Initial REMS approval: 02/2014

Most recent modification: 06/2014

BLA 125390
MYALEPT™ (metreleptin)

Drug Class: Recombinant human leptin analog

Manufactured for Amylin Pharmaceuticals LLC[1]
1800 Concord Pike
P.O Box 8355
Wilmington, DE, 19803-8355
1-800-236-9933

MYALEPT is marketed and distributed by: AstraZeneca Pharmaceuticals LP
1800 Concord Pike
P.O Box 8355
Wilmington, DE, 19803-8355
1-800-236-9933

RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOALS

The goal of the MYALEPT REMS is to mitigate (1) the risks of serious adverse sequelae (such as severe infections, excessive weight gain, glucose intolerance, diabetes mellitus) due to the development of anti-metreleptin antibodies that neutralize endogenous leptin and/or MYALEPT, and (2) the risk of lymphoma by:

- Educating prescribers about the development of neutralizing anti-metreleptin antibodies, the serious adverse sequelae that may result from these antibodies, and the risk for lymphoma associated with MYALEPT
- Limiting the population exposed to MYALEPT by requiring prescriber certification, pharmacy certification, and prescriber attestation that each patient has a diagnosis consistent with the approved indication

[1] Amylin Pharmaceuticals, LLC (Amylin Pharmaceuticals) is the licensee under BL 125390. Although Amylin Pharmaceuticals and AstraZeneca Pharmaceuticals LP have a contractual agreement under which AstraZeneca Pharmaceuticals LP is to carry out the responsibilities under the REMS for MYALEPT on behalf of Amylin Pharmaceuticals, Amylin Pharmaceuticals retains primary responsibility for all actions described in the REMS.

II. REMS ELEMENTS

A. Elements to Assure Safe Use (ETASU)

1. **Healthcare Providers (HCPs) who prescribe MYALEPT are specially certified.**

   a. Amylin Pharmaceuticals will ensure that HCPs who prescribe MYALEPT are specially certified.

   b. To become specially certified to prescribe MYALEPT, prescribers must enroll in the MYALEPT REMS Program. Prescribers must complete the following requirements:

      i. review the Prescribing Information

      ii. complete the Prescriber Training Module

      iii. complete and sign the *Prescriber Enrollment Form* and submit it to the MYALEPT REMS Program.

   c. Amylin Pharmaceuticals will:

      i. Ensure that the *Prescriber Training Module* and the *Prescriber Enrollment Form* are available on the MYALEPT REMS Program website (www.MYALEPTREMS.com) or can be obtained by contacting the MYALEPT REMS Program by phone at 1-855-6MYALEPT.

      ii. Ensure that prescribers complete the *Prescriber Training Module* and the *Prescriber Enrollment Form* before activating prescribers' certification in the MYALEPT REMS Program.

      iii. Ensure that prescribers are notified when they have been successfully certified by the MYALEPT REMS Program.

      iv. Inform certified prescribers following substantial changes to the MYALEPT REMS or MYALEPT REMS Program; substantial changes include significant changes to the operation of the MYALEPT REMS Program or changes to the Prescribing Information that affect the risk-benefit profile of MYALEPT.

      v. Communicate information about the risks and MYALEPT REMS Program requirements to prescribers through the MYALEPT REMS Program website and MYALEPT REMS introductory information sheet titled *MYALEPT REMS Program: An Introduction*. Amylin Pharmaceuticals will provide the *REMS Program: An Introduction*, *Prescriber Training Module, Prescriber Enrollment Form,* and the Prescribing Information to prescribers who (1) attempt to prescribe MYALEPT and are not yet certified, or (2) inquire about how to become certified.

   The following materials are part of the REMS and are appended:

   - *Prescriber Training Module*
   - *Prescriber Enrollment Form*
   - *MYALEPT REMS Program: An Introduction*

Reference ID: 3534419

- *MYALEPT REMS Program website*

2. Pharmacies that dispense MYALEPT are specially certified.

a. Amylin Pharmaceuticals will ensure that MYALEPT is dispensed only by specially certified pharmacies.

To become certified to dispense MYALEPT, each pharmacy representative must agree to the following:

i. to educate all pharmacy staff involved in the dispensing of MYALEPT on the MYALEPT REMS Program requirements

ii. to put processes and procedures in place to verify, prior to dispensing MYALEPT, that:

1) the prescriber is certified in the MYALEPT REMS Program

2) the *MYALEPT REMS Prescription Authorization Form* is received for each new prescription

iii. to be audited to ensure that all processes and procedures are in place and are being followed for the MYALEPT REMS Program

iv. to provide prescription data to the MYALEPT REMS Program, and

v. to refrain from reselling or transferring MYALEPT to other pharmacies or distributors.

The following material is part of the REMS and appended:

- *MYALEPT REMS Prescription Authorization Form*

Reference ID: 3534419

3. **MYALEPT is dispensed only to patients with evidence or other documentation of safe-use conditions.**

a. MYALEPT is dispensed only to patients whose prescribers are specially certified in the MYALEPT REMS Program and attest on the MYALEPT REMS Prescription Authorization Form that:

i. They understand that MYALEPT is indicated as an adjunct to diet as replacement therapy to treat the complications of leptin deficiency in patients with congenital or acquired generalized lipodystrophy.

ii. They affirm that their patient has a clinical diagnosis consistent with the approved indication, and that the patient (or caregiver) has been properly informed of the benefits and risks of MYALEPT therapy.

iii. They understand that MYALEPT is not indicated for the treatment of complications of partial lipodystrophy.

iv. They understand that MYALEPT is not indicated for the treatment of liver disease, including non-alcoholic steatohepatitis (NASH).

v. They understand that MYALEPT is not indicated for use in patients with HIV-related lipodystrophy.

vi. They understand that MYALEPT is not indicated for use in patients with metabolic disease, including diabetes mellitus and hypertriglyceridemia, without concurrent evidence of congenital or acquired generalized lipodystrophy.

vii. They understand that MYALEPT is contraindicated in patients with general obesity not associated with congenital leptin deficiency.

viii. They understand that MYALEPT is associated with serious adverse events due to the development of anti-metreleptin antibodies that neutralize endogenous leptin and/or MYALEPT.

ix. They agree to test for neutralizing antibodies to MYALEPT if a patient experiences severe infections or if they suspect MYALEPT treatment is no longer working (e.g., loss of glycemic control, increased triglycerides).

x. They understand that MYALEPT is associated with a risk of lymphoma.

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xi. They understand it is important to carefully consider treatment with MYALEPT in patients with significant hematologic abnormalities and/or acquired generalized lipodystrophy

B. Implementation System

1. Amylin Pharmaceuticals will ensure that MYALEPT is distributed to and dispensed only by certified pharmacies.
2. Amylin Pharmaceuticals will maintain, monitor, and evaluate the implementation of the MYALEPT REMS Program.
   a. Amylin Pharmaceuticals will maintain a secure, validated database of certified prescribers and pharmacies in the MYALEPT REMS Program. Amylin Pharmaceuticals will send confirmation of certification to each certified pharmacy.
   b. Amylin Pharmaceuticals will maintain a MYALEPT REMS Program Call Center to support patients, prescribers, and pharmacies interfacing with the MYALEPT REMS.
   c. Amylin Pharmaceuticals will ensure that all materials listed in or appended to the MYALEPT REMS Program will be available through the MYALEPT REMS Program website (www.MYALEPTREMS.com) or by calling the MYALEPT REMS Program Call Center at 1-855-6MYALEPT.
   d. If there are substantive changes to the MYALEPT REMS or MYALEPT REMS Program, Amylin Pharmaceuticals will update all affected materials, and notify enrolled prescribers and certified pharmacies, as applicable. Substantive changes are defined as significant changes to the operation of the MYALEPT REMS Program or changes to the Prescribing Information that affect the risk-benefit profile of MYALEPT.
   e. Amylin Pharmaceuticals will monitor and audit the certified pharmacies within 180 days after the pharmacy is certified to ensure that all processes and procedures are in place and functioning to support the requirements of the MYALEPT REMS Program. Thereafter, Amylin Pharmaceuticals will include the certified pharmacies in the company's annual audit plan. Corrective action will be instituted by Amylin Pharmaceuticals if noncompliance is found.
   f. Based on monitoring and evaluation of the MYALEPT REMS elements to assure safe use, Amylin Pharmaceuticals will take reasonable steps to improve implementation of these elements and to maintain compliance with the MYALEPT REMS Program requirements, as applicable.

C. Timetable for Submission of Assessments

Amylin Pharmaceuticals will submit REMS Assessments to the FDA 6 months, 12 months, and annually thereafter from the date of the initial REMS approval. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting

Reference ID: 3534419

interval covered by each assessment should conclude no earlier than 60 days before the submission date for that assessment. Amylin Pharmaceuticals will submit each assessment so that it will be received by the FDA on or before the due date.

Reference ID: 3534419

myalept™
(metreleptin) For Injection
11.3 mg per vial

MYALEPT™ REMS Program Prescriber Enrollment Form

MYALEPT will be available only through the MYALEPT REMS Program. To prescribe MYALEPT, a prescriber must: (1) review the Prescribing Information, review and complete the Prescriber Training Module, (2) complete this one-time MYALEPT REMS Program Prescriber Enrollment Form, and (3) complete and submit a MYALEPT REMS Prescription Authorization Form for each new prescription.

Complete this enrollment form and fax it to the MYALEPT REMS Program at 1-877-328-9682.

Prescriber Information (Please Print *indicates a required field.)

Full Name (first, middle, last)*

Credentials*
☐ MD ☐ DO ☐ NP ☐ PA ☐ Other (specify) _____

Physician Specialty* ☐ Endocrinology ☐ Family Medicine ☐ Cardiology ☐ General Internal Medicine ☐ Pediatrics ☐ Other _____

Who do you treat?
☐ Adults ☐ Pediatrics ☐ Both

Practice / Facility Name

Address 1*

Address 2 (optional)	City*	State*	ZIP code*

Phone number*	Alternate phone number*	Fax number*

Email*	NPI #*

Practice Setting ☐ Solo private practice ☐ Group private practice ☐ Academic/ Hospital affiliated practice ☐ Government Institution ☐ Other _____

Office Contact

Full Name (first, middle, last)*

Phone number (if different from above)	Fax number (if different from above)	Email* (if office contact is provided)

Prescriber Attestation. By completing this form, I attest that:

- I understand that MYALEPT is indicated as an adjunct to diet as replacement therapy to treat the complications of leptin-deficiency in patients with congenital or acquired generalized lipodystrophy.
- I understand that MYALEPT is available only through the MYALEPT REMS Program and that I must comply with the program requirements in order to prescribe MYALEPT.
- I have completed the MYALEPT REMS Prescriber Training Module.
- I understand that MYALEPT is associated with serious adverse events due to the development of anti-metreleptin antibodies that neutralize endogenous leptin and/or MYALEPT.
- I agree to test for neutralizing antibodies in patients who experience severe infections or if I suspect MYALEPT is no longer working (e.g., loss of glycemic control, or increases in triglycerides).
- I understand that MYALEPT is associated with a risk of lymphoma.
- I will carefully consider the risks of treatment with MYALEPT in patients with significant hematologic abnormalities and/or acquired generalized lipodystrophy.
- I understand that MYALEPT is not indicated for the treatment of complications of partial lipodystrophy.
- I understand that MYALEPT is not indicated for the treatment of liver disease, including non-alcoholic steatohepatitis (NASH).
- I understand that MYALEPT is not indicated for use in patients with HIV-related lipodystrophy.
- I understand that MYALEPT is not indicated for use in patients with metabolic disease, including diabetes mellitus and hypertriglyceridemia without concurrent evidence of congenital or acquired generalized lipodystrophy.
- I understand that MYALEPT is contraindicated in patients with general obesity not associated with congenital leptin deficiency.
- I agree that personnel from the MYALEPT REMS Program may contact me to gather further information or resolve discrepancies or to provide other information related to MYALEPT or the MYALEPT REMS Program.
- I will complete and submit a MYALEPT REMS Program Prescription Authorization Form for each new prescription.
- I agree that AstraZeneca, its agents and contractors such as the pharmacy providers, may contact me via phone, mail, or email to survey me on the effectiveness of the program requirements for the MYALEPT REMS Program.

Signature* _____ **Date*** _____

If you have any questions, please contact the MYALEPT REMS Program.
Phone number: 1-855-669-2537 | Fax number: 1-877-328-9682 | www.MYALEPTREMS.COM

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MYALEPT is manufactured for Amylin Pharmaceuticals and distributed by AstraZeneca Pharmaceuticals LP.

myalept™
(metreleptin) For Injection
11.3 mg per vial

MYALEPT™ REMS Program
Prescription Authorization Form

Instructions: Complete both **pages** of this form for each new prescription. All fields are required. Please Print.
Please FAX completed form to MYALEPT REMS Program at 1-877-328-9682.
The prescription for MYALEPT is only valid if received by fax.
For New York prescribers: In addition to this completed form, provide New York specific prescription blanks.

Patient Information

Full Name (first, middle, last)		Gender ☐ Male ☐ Female	Date of Birth
Address		City	State / ZIP code
Preferred phone number	Alternate phone number		Preferred time to contact: (check one) ☐ Day ☐ Evening
Email		Alternate contact/phone #	
Parent/Guardian (if applicable)			

Insurance Information Please copy and attach the front and back of the insurance card.

Insurance company phone number	
Insured Name	Relationship to patient
Insured Employer	
Prescription card ☐ Yes ☐ No If yes, carrier _____	
Policy Number	
Is the patient eligible for Medicare? ☐ Yes ☐ No	
Policy number	Group Number

Shipping Information

Full Name (first, middle, last)			
Address (if different from above)	City	State	ZIP code
Send initial shipment to prescribing doctor's office ☐ Yes ☐ No			

Prescriber Information

Full Name (first, middle, last)			
Practice / Facility Name		Office Contact Person	
Address 1			
Address 2		City	State / ZIP code
Office Phone number	Office Fax number	License #	NPI #

Continue to page 2 to complete prescription.

The MYALEPT REMS Program may be found at www.MYALEPTREMS.com or by calling 1-855-669-2537.

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myalept™
(metreleptin) For Injection
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MYALEPT™ REMS Program
Prescription Authorization Form

Attestation of REMS Requirements. By completing this form, I attest that:

- I understand that MYALEPT is indicated as an adjunct to diet as replacement therapy to treat the complications of leptin-deficiency in patients with congenital or acquired generalized lipodystrophy.
- I affirm that my patient has a clinical diagnosis consistent with generalized lipodystrophy, and that my patient (or their caregiver) has been properly informed of the benefits and risks of MYALEPT therapy.
- I understand that MYALEPT is not indicated for the treatment of complications of partial lipodystrophy.
- I understand that MYALEPT is not indicated for the treatment of liver disease, including non-alcoholic steatohepatitis (NASH).
- I understand that MYALEPT is not indicated for use in patients with HIV-related lipodystrophy.
- I understand that MYALEPT is not indicated for use in patients with metabolic disease including diabetes mellitus and hypertriglyceridemia without concurrent evidence of congenital or acquired generalized lipodystrophy.
- I understand that MYALEPT is contraindicated in patients with general obesity not associated with congenital leptin deficiency.
- I understand that MYALEPT is associated with serious adverse events due to the development of anti-metreleptin antibodies that neutralize endogenous leptin and/or MYALEPT.
- I agree to test for neutralizing antibodies in patients who experience severe infections or if I suspect MYALEPT is no longer working (e.g., loss of glycemic control, or increases in triglycerides).
- I understand that MYALEPT is associated with a risk of lymphoma.
- I understand I must carefully consider the risks of treatment with MYALEPT in patients with significant hematological abnormalities and/or acquired generalized lipodystrophy.

Physician Signature: _____ **Date:** _____

Starting Dose: [ ] 0.06 mg/kg [ ] 2.5 mg [ ] 5 mg [ ] **Maintenance Dose:** _____			
Patient Weight	Days Supply	Refills #	
Directions (e.g., by subcutaneous injection once daily)			
List or Attach a List of Concomitant Medications		Allergies	
Full Name (first, middle, last)			
Full Name (first, middle, last)			
Address			
City	State	ZIP code	Office Phone
License #		NPI #	

Physician Signature: _____ **Date** _____ **Physician Signature:** _____ **Date** _____

Product Selection Permitted **Dispense as Written**

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The following is a prescription form for the required ancillary supplies for MYALEPT reconstitution and administration. This can be faxed back to 1-877-328-9682 with the rest of this page and the previous page, or torn off and given to your patient to fill at another pharmacy.

Patient Information			
Full Name (first, middle, last)			
MYALEPT Supplies Prescription			
Required supplies (please note - the maximum number per supply is specified below. Pharmacy will adjust to individual patient needs.)			
For Reconstitution ☐ 5 of 30 mL vials of BWFI Refills # _____ ☐ 31 of 5 mL vials of SWFI (use for neonates and infants) Refills # _____ ☐ 62 of 3mL syringe (22G x 1 in. needle) Refills # _____		**For Administration** ☐ 62 of 1mL tuberculin syringe (26 G x 3/8 in. needle) Refills # _____	
Prescriber Information			
Full Name (first, middle, last)			
Address			
City	State	ZIP code	Office Phone
License #		NPI #	

Physician Signature: _____ **Date** _____ **Physician Signature:** _____ **Date** _____

Product Selection Permitted **Dispense as Written**

Risk **E**valuation and **M**itigation **S**trategy (REMS) Program

Prescriber Training Module

Contents

- Introduction
- MYALEPT™ (metreleptin) for injection Product Information
  - **Boxed Warning:** risk of development of anti-metreleptin antibodies that neutralize endogenous leptin and/or MYALEPT
  - **Boxed Warning:** risk of lymphoma
  - Appropriate patient selection
- MYALEPT REMS Program Information
- Knowledge Assessment

Introduction

Introduction

MYALEPT™ (metreleptin) for injection is available only through a restricted program called the MYALEPT REMS Program.

- Prescribers must complete this training module and enroll in the MYALEPT REMS Program prior to prescribing MYALEPT.

The purpose of this training module is to educate prescribers about

- the development of anti-metreleptin antibodies that neutralize endogenous leptin and/or MYALEPT and the serious adverse events that may result from these antibodies,
- the risk of lymphoma, and
- appropriate patient selection

Because of these risks, appropriate patient selection consistent with the approved indication for MYALEPT is very important.

MYALEPT™ (metreleptin) for injection Product Information

Indication

MYALEPT™ (metreleptin) for injection is indicated as an adjunct to diet as replacement therapy to treat the complications of leptin deficiency in patients with congenital or acquired **generalized lipodystrophy**

Serious Risks Associated with MYALEPT

Serious Risks Associated with MYALEPT

1. Development of anti-metreleptin antibodies that neutralize endogenous leptin and MYALEPT
2. Lymphoma

Boxed Warning: Anti-metreleptin Antibodies with Neutralizing Activity - Serious Adverse Events

- Anti-metreleptin antibodies with neutralizing activity associated with adverse events consistent with loss of endogenous leptin activity and/or loss of efficacy have been identified among patients with generalized lipodystrophy
  - 2 of 33 patients who underwent antibody testing
    1. tested positive for anti-metreleptin antibodies with neutralizing activity

    and

    2. reported adverse events consistent with neutralizing activity, including severe infections, loss of glycemic control, and increases in triglycerides

Boxed Warning: Anti-metreleptin Antibodies with Neutralizing Activity - Serious Adverse Events (continued)

- In other populations
  - 3 of 563 patients who underwent antibody testing
    1. tested positive for anti-metreleptin antibodies with neutralizing activity

    and

    2. reported adverse events consistent with neutralizing activity, including excessive weight gain and development of glucose intolerance or diabetes mellitus

The clinical implications associated with development of anti-metreleptin antibodies with neutralizing activity are not well-characterized at this time due to the small number of reports.

Antibody Testing in MYALEPT Trials - Data

- Anti-metreleptin antibodies were detected in 84% (36/43) of patients with generalized lipodystrophy studied in the MYALEPT trials
- Total anti-metreleptin antibody titers ranged between 1:5 and 1:1,953,125
- Anti-metreleptin antibodies with neutralizing activity associated with adverse events consistent with loss of endogenous leptin activity and/or loss of MYALEPT efficacy were observed in 6% (2/33) of the patients tested

Antibody Testing in MYALEPT Trials - Limitations

- The immunogenicity assays utilized in clinical trials lacked sensitivity, resulting in potential underestimation of the number of samples positive for anti-metreleptin antibodies with neutralizing activity
  - The observed incidence of an antibody assay (including neutralizing antibody assays) positivity may be influenced by several factors including assay sensitivity and specificity, assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease.

Antibody Testing in MYALEPT Trials – Limitations (continued)

- Antibody testing was not performed uniformly in the MYALEPT trials. The incompleteness of the current immunogenicity database precludes understanding of the magnitude and persistence of the observed anti-metreleptin antibody responses.

- Comparison of the incidence of antibodies to metreleptin with the incidence of antibodies to other products may be misleading.

Neutralizing Activity - What is My Role?

- Test for neutralizing activity in patients who experience severe infections or if you suspect that MYALEPT is no longer working.
- Contact AstraZeneca at 1-866-216-1526 for instructions on how to submit samples for neutralizing antibody testing. The assay is not commercially available.

AstraZeneca will ask you to:

1. Obtain written consent from your patient to release the sample and send a copy of the consent to AstraZeneca.
2. Complete a questionnaire to explain why you are requesting neutralizing activity testing and send it to AstraZeneca.
3. Send the sample to the designated laboratory for testing.
   - The results are generally available within 60 days
4. AstraZeneca will contact you to provide and discuss the results.

Boxed Warning: Lymphoma

- Three cases of T-cell lymphoma have been reported in the MYALEPT lipodystrophy program
  - All 3 patients had **acquired generalized lipodystrophy (out of a total of 20 patients with acquired generalized lipodystrophy).**
    - Two of these patients were diagnosed with peripheral T-cell lymphoma while receiving MYALEPT.
    - Both had immunodeficiency and significant hematologic abnormalities, including severe bone marrow abnormalities, before the start of MYALEPT treatment.
    - A separate case of anaplastic large cell lymphoma was reported in a patient receiving MYALEPT <u>who did not have hematological abnormalities before treatment.</u>

Lymphoma – What is My Role?

- Take a careful medical history for past or current hematologic abnormalities
- Carefully consider the benefits and risks of treatment with MYALEPT in patients with
  - significant hematologic abnormalities, and/or
  - acquired generalized lipodystrophy

Adverse Reaction Reporting

To report SERIOUS ADVERSE REACTIONS, please call/contact:

- 1-855-669-2537 and/or
- FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

Appropriate Patient Selection

Appropriate Patient Selection

Contraindication – General Obesity

MYALEPT is contraindicated in patients with general obesity not associated with congenital leptin deficiency.

- MYALEPT has not been shown to be effective in treating general obesity, and the development of anti-metreleptin antibodies with neutralizing activity has been reported in obese patients treated with MYALEPT
- Adverse events consistent with loss of endogenous leptin activity have been identified in three patients without lipodystrophy who received metreleptin (excessive weight gain, development of glucose intolerance or diabetes mellitus).

The clinical implications associated with development of anti-metreleptin antibodies with neutralizing activity are not well-characterized at this time due to the small number of reports.

Appropriate Patient Selection

Important Limitations of Use

- **The safety and effectiveness of MYALEPT for the following conditions have <u>not</u> been established**
  - The treatment of complications of partial lipodystrophy
  - The treatment of liver disease including non-alcoholic steatohepatitis (NASH)

- **MYALEPT <u>is not indicated for use</u> in patients with**
  - HIV-related lipodystrophy
  - Metabolic disease including diabetes mellitus and hypertriglyceridemia, without concurrent evidence of congenital or acquired generalized lipodystrophy.

MYALEPT™ (metreleptin) for injection
REMS PROGRAM INFORMATION

MYALEPT™ (metreleptin) for injection REMS Program

Key program elements:

- Certification of Prescribers of MYALEPT
  - Certification consists of training, and enrolling in the MYALEPT REMS Program.
- Completion of a Prescription Authorization Form for each new prescription
- Restricted distribution of MYALEPT through certified pharmacies.

MYALEPT™ (metreleptin) for injection REMS Program

Before prescribing MYALEPT, prescribers must complete the following steps:

1. Review the Prescribing Information and this Prescriber Training Module.
2. Complete, sign, and submit the one-time MYALEPT REMS Program Prescriber Enrollment Form.
3. Complete, sign, and submit the MYALEPT REMS Program Prescription Authorization Form for each new prescription.

Note: All Materials can be downloaded from the MYALEPT REMS website at: www.MYALEPTREMS.com

Or request these materials by calling 1-855-669-2537

1. Review Prescriber Education Materials

Review the following Prescriber Education Materials:

a) MYALEPT™ (metreleptin) for injection Prescribing Information

b) This Prescriber Training Module

2. Enroll in MYALEPT™ (metreleptin) for injection REMS Program

To enroll in the MYALEPT REMS Program:

- Download the MYALEPT REMS Program Prescriber Enrollment Form at www.MYALEPTREMS.com or request a copy by calling 1-855-669-2537
- Complete the enrollment form
- Sign & submit the enrollment form
  - Fax to 1-877-328-9682

3. Submit Prescription Authorization Form

When prescribing MYALEPT™ (metreleptin) for injection, a prescriber must complete a Prescription Authorization Form for each new prescription.

As part of completing the Prescription Authorization Form, you attest that:

- I understand that MYALEPT is indicated as an adjunct to diet as replacement therapy to treat the complications of leptin-deficiency in patients with congenital or acquired generalized lipodystrophy.

- I affirm that my patient has a clinical diagnosis consistent with generalized lipodystrophy, and that my patient (or their caregiver) has been properly informed of the benefits and risks of MYALEPT therapy.

3. Submit Prescription Authorization Form (continued)

- I understand that MYALEPT is not indicated for the treatment of complications of partial lipodystrophy.
- I understand that MYALEPT is not indicated for the treatment of liver disease, including non-alcoholic steatohepatitis (NASH).
- I understand that MYALEPT is not indicated for use in patients with HIV-related lipodystrophy.
- I understand that MYALEPT is not indicated for use in patients with metabolic disease including diabetes mellitus and hypertriglyceridemia without concurrent evidence of congenital or acquired generalized lipodystrophy.

3. Submit Prescription Authorization Form (continued)

- I understand that MYALEPT is contraindicated in patients with general obesity not associated with congenital leptin deficiency.
- I understand that MYALEPT is associated with serious adverse events due to the development of anti-metreleptin antibodies that neutralize endogenous leptin and/or MYALEPT.
- I agree to test for neutralizing antibodies in patients who experience severe infections or if I suspect MYALEPT is no longer working (e.g., loss of glycemic control, or increases in triglycerides).
- I understand that MYALEPT is associated with a risk of lymphoma.
- I understand I must carefully consider the risks of treatment with MYALEPT in patients with significant hematologic abnormalities and/or acquired generalized lipodystrophy.

3. Submit Prescription Authorization Form

Each new prescription for MYALEPT must be written using the MYALEPT Prescription Authorization Form.

1. Download the Prescription Authorization Form at www.MYALEPTREMS.com or request a copy by calling 1-855-669-2537
2. Complete the Prescription Authorization Form
3. Sign & submit the Prescription Authorization Form
   - Fax to 1-877-328-9682

Knowledge Assessment

Knowledge Assessment

- The following questions about MYALEPT™ (metreleptin) for injection are provided to reinforce learning.
- If you have difficulty answering these questions, review the previous slides and refer to the Prescribing Information.

Knowledge Assessment

1. Which of the following statements is true?
   - ☐ MYALEPT (metreleptin) for injection is indicated for use in patients with HIV-related lipodystrophy.
   - ☐ MYALEPT is indicated for use in patients with metabolic disease, including diabetes mellitus and hypertriglyceridemia, without concurrent evidence of inherited or acquired generalized lipodystrophy.
   - ☐ MYALEPT is a recombinant analog of murine leptin.
   - ☐ MYALEPT is indicated as an adjunct to diet as replacement therapy to treat the complications of leptin deficiency in patients with congenital or acquired generalized lipodystrophy.

Knowledge Assessment

1. Which of the following statements is true?
   - ☐ MYALEPT (metreleptin) is indicated for use in patients with HIV-related lipodystrophy.
   - ☐ MYALEPT is indicated for use in patients with metabolic disease, including diabetes mellitus and hypertriglyceridemia, without concurrent evidence of inherited or acquired generalized lipodystrophy.
   - ☐ MYALEPT is a recombinant analog of murine leptin.
   - ✓ **MYALEPT is indicated** as an adjunct to diet as replacement therapy to treat the complications of leptin deficiency in patients with congenital or acquired generalized lipodystrophy.

Answer: MYALEPT is indicated as an adjunct to diet as replacement therapy to treat the complications of leptin deficiency in patients with congenital or acquired generalized lipodystrophy

(continued on next slide)

(continued from previous slide)

- **The safety and effectiveness of MYALEPT for the following conditions have not been established**
  - The treatment of complications of partial lipodystrophy
  - The treatment of liver disease including non-alcoholic steatohepatitis (NASH)

- **MYALEPT <u>is not indicated for use</u> in patients with**
  - HIV-related lipodystrophy
  - Metabolic disease including diabetes mellitus and hypertriglyceridemia, without concurrent evidence of congenital or acquired generalized lipodystrophy.

- **MYALEPT is <u>contraindicated</u> in patients with general obesity not associated with congenital leptin deficiency.**

Knowledge Assessment

2. The risks and benefits of MYALEPT™ (metreleptin) for injection treatment should be carefully considered in patients with significant hematologic abnormalities (for example, leukopenia, neutropenia, bone marrow abnormalities, lymphoma and/or lymphadenopathy) and/or acquired generalized lipodystrophy.

   ☐ True

   ☐ False

Knowledge Assessment

2. The risks and benefits of MYALEPT™ (metreleptin) for injection treatment should be carefully considered in patients with significant hematologic abnormalities (for example, leukopenia, neutropenia, bone marrow abnormalities, lymphoma and/or lymphadenopathy) and/or acquired generalized lipodystrophy.

   ✓ True

   ☐ False

Answer:
- Peripheral T-cell lymphoma was diagnosed in two patients with acquired generalized lipodystrophy while receiving MYALEPT.
  - Both had immunodeficiency and significant hematologic abnormalities including severe bone marrow abnormalities before the start of MYALEPT treatment.
- A separate case of anaplastic large cell lymphoma was reported in a patient with acquired generalized lipodystrophy who did not have hematologic abnormalities before MYALEPT treatment.

Knowledge Assessment

3. Developing neutralizing activity to metreleptin could:
   - ☐ affect endogenous leptin
   - ☐ result in loss of efficacy
   - ☐ both of the above
   - ☐ none of the above

Knowledge Assessment

3. Developing neutralizing activity to metreleptin could:
   - ☐ affect endogenous leptin
   - ☐ result in loss of efficacy
   - ✓ both of the above
   - ☐ none of the above

Answer: Developing neutralizing activity to metreleptin could affect endogenous leptin and could result in loss of efficacy.

Knowledge Assessment

4. If a patient is experiencing severe infections and/or I suspect Myalept is no longer working, I will contact AstraZeneca for instructions on how to send a blood sample to test for anti-metreleptin antibodies with neutralizing activity.

   - ☐ True
   - ☐ False

Knowledge Assessment

4. If a patient is experiencing severe infections and/or I suspect Myalept is no longer working, I will contact AstraZeneca for instructions on how to send a blood sample to test for anti-metreleptin antibodies with neutralizing activity.

   ✓ True

   ☐ False

Answer: If you suspect your patient is experiencing complications from the development of anti-metreleptin neutralizing antibodies, you can submit a request and obtain results from AstraZeneca at no cost.

1. Call 1-866-216-1526
   - AstraZeneca will provide you information on the requirements for sample collection and shipment.
2. AstraZeneca will instruct you to:
   a. Obtain written consent from your patient to release the sample and send a copy of the consent to AstraZeneca.
   b. Complete a questionnaire to explain why you are requesting neutralizing activity testing.
   c. Send the sample and paperwork to the designated laboratory for testing.
   - The results are generally available within 60 days
3. AstraZeneca will contact you to provide and discuss the results.

Knowledge Assessment

5. How often should the Prescription Authorization Form be completed?
   - ☐ Each new prescription
   - ☐ Only on the first prescription
   - ☐ Every refill
   - ☐ Once a year

Knowledge Assessment

5. How often should the Prescription Authorization Form be completed?
   - ✓ Each new prescription
   - ☐ Only on the first prescription
   - ☐ Every refill
   - ☐ Once a year

Answer: For each new prescription, the prescriber must submit a Prescription Authorization Form.

Knowledge Assessment

6. MYALEPT™ (metreleptin) for injection is available only through certified pharmacies.
   - ☐ True
   - ☐ False

Knowledge Assessment

6. MYALEPT™ (metreleptin) for injection is available only through certified pharmacies.
   - ✓ True
   - ☐ False

Answer: MYALEPT is available only through pharmacies that are specially certified and agree to follow REMS requirements. For a list of certified pharmacies call: 1-855-669-2537.

Completion of Training for the MYALEPT™ (metreleptin) for injection REMS Program

You have completed training for the MYALEPT REMS Program.

To enroll in the MYALEPT REMS Program, complete the Enrollment Form and return via fax at 1-877-328-9682.

For more information on the MYALEPT REMS Program, please call 1-855-669-2537 or visit www.MYALEPTREMS.com.

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MYALEPT is manufactured for Amylin Pharmaceuticals and distributed by AstraZeneca Pharmaceuticals LP.

myalept™
(metreleptin) For Injection

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MYALEPT REMS Program: An Introduction

What is the MYALEPT REMS (Risk Evaluation and Mitigation Strategy) Program?

A REMS is a strategy to manage known or potential risks associated with a drug, and is required by the FDA to ensure that the benefits of the drug outweigh its risks. MYALEPT is available only under a restricted program called the MYALEPT REMS Program because of:

- the development of anti-metreleptin antibodies that neutralize endogenous leptin and/or MYALEPT and the serious adverse events that may result
- the risk of lymphoma.

Because of these risks, appropriate patient selection consistent with the approved indication for MYALEPT is very important.

MYALEPT REMS Program Requirements

- Certification of Prescribers of MYALEPT
- Completion of a Prescription Authorization Form for each new prescription
- Restricted distribution of MYALEPT through certified pharmacies

Certification of Prescribers of MYALEPT

1. Review the Prescribing Information and MYALEPT Prescriber Training Module
2. Complete, sign, and submit the one-time MYALEPT REMS Program Prescriber Enrollment Form

All Materials can be downloaded from the MYALEPT REMS website at: www.MYALEPTREMS.com.
Or request these materials by calling 1-855-669-2537.

Completion of Prescription Authorization Form

Each new prescription for MYALEPT must be written using the MYALEPT Prescription Authorization Form.

- Download the Prescription Authorization Form at www.MYALEPTREMS.com or request a copy by calling 1-855-669-2537
- Complete the Prescription Authorization Form

Restricted Distribution of MYALEPT through Certified Pharmacies

Prescription Authorization Form must be signed and submitted by:
Fax to 1-877-328-9682

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MYALEPT™ REMS Program

Program Requirements | Training & Enrollment

A Risk Evaluation and Mitigation Strategy (REMS) is a strategy to manage known or potential serious risks associated with a drug product and is required by the Food and Drug Administration (FDA) to ensure that the benefits of a drug outweigh its risks.

AstraZeneca has worked with the FDA to develop the MYALEPT REMS Program:

To educate prescribers about
- the development of anti-metreleptin antibodies that neutralize endogenous leptin and/or MYALEPT and the serious adverse events that may result from these antibodies,
- the risk of lymphoma, and
- appropriate patient selection

Program Requirements

MYALEPT is available only through the MYALEPT REMS Program. The MYALEPT REMS Program requirements include:

For Prescribers:

- **Certification** of prescribers of MYALEPT
  - Certification consists of completion of **training, and enrollment** in the MYALEPT REMS Program
- **Completion** of a Prescription Authorization form for **each** new prescription

Find out more about Training & Enrollment.

For Pharmacies:

- **Restricted distribution** of MYALEPT to patients with completed Prescription Authorization Forms from prescribers who are certified in the MYALEPT REMS Program

Training & Enrollment

Healthcare providers who prescribe MYALEPT must review the prescriber training materials to enroll in the MYALEPT REMS Program.

Steps to Prescriber Certification

1. **Review the Prescriber Education Materials**
   - MYALEPT Prescribing Information
   - Prescriber Training Module
2. **Complete and submit the MYALEPT REMS Program Prescriber Enrollment Form**
   - Print and sign the Prescriber Enrollment Form or request a copy by calling 1-855-669-2537
   - Submit the form via:
     - Fax to 1-877-328-9682

By completing the Prescriber Enrollment Form, the prescriber agrees to comply with the MYALEPT REMS Program requirements. A confirmation of your certification in the MYALEPT REMS program will be sent to you so you can begin to prescribe MYALEPT.

Reporting Adverse Reactions

Healthcare providers should report all suspected adverse events.
Please contact the company at **1-855-669-2537** or FDA at **1-800-FDA-1088** or www.fda.gov/medwatch.com.

REMS Materials

- PDF MYALEPT REMS Program: An Introduction
- PDF MYALEPT REMS Program Prescriber Training Module
- PDF MYALEPT REMS Program Prescriber Enrollment Form
- PDF MYALEPT REMS Program Prescription Authorization Form
- PDF Prescribing Information

MYALEPT REMS Program Contact Us

Phone: 1-855-669-2537
Fax: 1-877-328-9682
Hours of Operation:
Monday - Friday,
8:00am-8:00pm
Eastern Time

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